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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,104	03/27/2001	J. Don Chen	UMG-030	4327

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/819,104	CHEN, J. DON	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 9/20/2004.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 19-26 and 30-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 19-26 is/are rejected.

7)☒ Claim(s) 30-34 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 08042004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 19-26, 30-34 are pending and under consideration.

Response to Amendment

The objection to the Title has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 19-26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues are set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-26 stand rejected, and new claim 30 is rejected, under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a method for identifying a compound which binds to a polypeptide with the sequence as set forth in SEQ ID NO: 2, does not reasonably provide enablement for methods of identification of compounds that bind to SMRTe polypeptides, or to polypeptides which are encoded by nucleic acids which hybridize to complements of SEQ ID NO: 2 for reasons of record set forth in the Office Action of 2/4/2004.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to methods of identification of compounds that bind to SMRTe polypeptides, and polypeptides which are encoded by nucleic acids which hybridize to complements of SEQ ID NO: 2. The Specification defines SMRTe polypeptides on page 26 as including biologically active portions and polypeptide fragments, and the term complement does not include any length limitation. The claims are thus directed to methods using variant polypeptides and Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SMRTe. Claims 19-26 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides encompassed by the claimed methods will retain the function or characteristics of a SMRTe polypeptide. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single

amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass methods using variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass methods using encoded polypeptides that the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to practice the claimed methods using the encompassed polypeptides. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polypeptides

that the specification only teaches one skilled in the art to test for functional variants. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polypeptide variants of SMRTe, and has not taught how to make polypeptide variants of SMRTe, it would require undue experimentation of one of skill in the art to practice the claimed methods.

Applicant argues that they describe in detail the structure and function of SMRTe polypeptides and in particular, the relevant SMRTe domains and the function of these domains, and that the SMRTe polypeptides are described as having a common functional characteristic such as gene transcription repressor activity, i.e. SMRTe activity. However, there are no structural or functional characteristics incorporated into the claim regarding the SMRTe polypeptides to be used in the claimed method. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, the Specification clearly sets forth that the term SMRTe encompasses fragments and variants of the SMRTe polypeptides, without setting forth any structural or functional limitations, thus the claims are not enabled.

Claims 19-26 stand rejected, and new claim 30 is rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 2/4/2004. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to methods of identification of compounds that bind to SMRTe polypeptides, and polypeptides which are encoded by nucleic acids which hybridize to complements of SEQ ID NO: 2. The Specification defines SMRTe polypeptides on page 26 as including biologically active portions and polypeptide fragments, and there is no length limitation for the complement of SEQ ID NO: 2 to which the encoding nucleic acid must bind, thus these are genus claims. The claims are directed to methods utilizing variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the SMRTe variants. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the

omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a

representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

In addition, due to the limitation of "allelic variant" recited in claim 8, from which claims 19-26 depend, a determination of what the claim as a whole covers indicates that elements which are not particularly described, e.g. the sequence of the claimed allelic variants, are encompassed by this claim. There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. A biomolecular sequence described only by a functional characteristic, in this case an allelic variant of a protein whose sequence is set forth in SEQ ID NO: 2, without any known or disclosed correlation between the function and the structure of the sequence is not a sufficient identifying characteristic. See University of California v. Eli Lilly and Co. 43 USPQ2d at 1406. There is no known or disclosed correlation between this function and the structure of the non-described allelic variants and the disclosed polypeptide with an amino acid sequence as set forth in SEQ ID NO: 2. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

Applicant argues that they have described in their Specification at least seven representative Species of polynucleotides encoding SMRTe polypeptides that fall within the claimed methods using a class of SMRTe polypeptides. The specification defines a SMRTe polypeptide as structurally comprising, e.g., an extended N-terminal region, of up to 1111 amino acids, and having several domains which can modulate gene expression in cells. However, these structural features are not set forth in the claim, nor is any function set forth for the variant polypeptides encompassed by the claims, since the Specification defines SMRTe polypeptides as

encompassing variants and fragments. While the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, since neither structural nor functional features are set forth for the polypeptide used in the claimed method, there is no correlation between structure and function, the method as claimed was not in possession of the Applicant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-26 stand rejected, and new claim 30 is rejected, under 35 U.S.C. 102(b) as being anticipated by WO 97/09418 (Evans et al.), for reasons of record set forth in the Office Action of 2/4/2004.

The claims are drawn to methods of identification of compounds that bind to SMRTe polypeptides, and polypeptides which are encoded by nucleic acids which hybridize to complements of SEQ ID NO: 2. The Specification defines SMRTe polypeptides on page 26 as including biologically active portions and polypeptide fragments, and there is no length limitation set forth for the complement to which the encoding nucleic acids must bind. The Evans reference teaches a nuclear co repressor which interacts with the retinoic acid receptor (page 2, lines 20-29). The amino acid sequence of the SMRT polypeptide is 57.5% identical to the polypeptide disclosed as SEQ ID NO: 2, and comprises sequence fragments identical to SEQ ID NO: 2 which are more than 15 amino acids in length (see Sequence Comparison A, attached).

The Evans reference also teaches methods of identifying compounds that bind to the SMRT protein (page 7, line 34 to page 9, line 27). Since the instant claims are drawn to methods utilizing a SMRTe polypeptide, for which no structural or functional limitations are set forth, the claims encompass the polypeptide as taught in the Evans reference, which also teaches methods of identifying compounds using the protein, the claims are anticipated.

Applicant argues that as amended, the present claims are drawn to methods that employ SMRTe polypeptides which, as defined in the specification, are distinct from SMRT polypeptides in that they, inter alia, comprise a large N-terminal extended region of structural and functional significance, or a portion thereof. However, the claims do not set forth these structural limitations, and limitations from the specification are not read into the claims. In re Van Geuns. Applicant further argues that the SMRT polypeptide of Evans simply lacks the structural and functional features of the SMRTe polypeptides of the claimed invention, however, the claims do not set forth any structural or functional limitations for the SMRTe polypeptides used in the claimed methods, thus the claims are anticipated.

Conclusion

Claims 19-26 are rejected.

Claims 30-34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 30, 2004

JOSEPH MURPHY
PATENT EXAMINER